Remarks

Claims 46, 72 and 73 are pending in this application. By this amendment, claim 46 has been amended. Support for this amendment can be found throughout the specification and in particular, page 14, lines 16-17, page 35, lines 27-39 and page 59, lines 12-15.

No new matter is added by this amendment. Consideration and allowance of the pending claims are requested.

Rejections under 35 U.S.C. §112, second paragraph

Claims 46, 72 and 73 are rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for reciting "binding of the HIV protein to the target protein" and "wherein the host protein is a protein encoded by a Rab9 target sequence comprises SEQ ID NO: 118." Claim 46 has been amended to recite "binding of the HIV protein to the host protein" and to "a human Rab9 target sequence." All references to SEQ ID NO: 118 have been removed. Exemplary human Rab9 target sequences are described in the specification such as on page 14, lines 16-17 and page 35, lines 27-39. Applicants believe these amendments render the pending 35 U.S.C. §112, second paragraph rejections moot and request that they be withdrawn.

Rejections under 35 U.S.C. §103(a)

Claims 46, 72 and 73 are rejected under 35 U.S.C. §103(a) as obvious over Wu *et al.* (U.S. Patent Application Publication 2003/0166870 A1) in view of Hanna *et al.* (*Proc. Nat. Acad. Sci.* 99: 7450-7454, 2002) and further in view of Munzy *et al.* (Accession number AC 079383, 2000, p. 1-64) as evidenced by Blot *et al.* (*J. Virology* 77: 6931-6945, 2003). Applicants traverse this rejection for at least the following reasons.

Wu *et al.* disclose methods of identifying an agent that decreases binding of HIV envelope protein to CCR5 chemokine receptor.

Hanna *et al.* identify the residues in the vesicle cargo selection protein TIP47 that are involved in the binding of Rab9.

Munzy *et al.* provides the Genbank accession number of AC079383 for Rab9.

Blot *et al.* investigate the role of TIP47 in the targeting of HIV type 1 envelope to the trans-Golgi network. Blot *et al.* teach that the binding of TIP47 to HIV type 1 envelope is required for envelope incorporation into virions and infectivity.

To establish a *prima facie* case of obviousness, the Examiner must identify all of the claimed elements in one or more prior art references and provide a motivation or suggestion to combine or modify the prior art references coupled with a reasonable expectation of success (M.P.E.P. §2143).

Cited References Fail to Teach all of the Claimed Elements

The Office has failed to establish a *prima facie* case of obviousness because all of the claim elements are not taught, suggested or disclosed by the cited references either alone or in combination. None of the references either alone or in combination disclose, suggest or render obvious a method of identifying a compound that decreases binding of an HIV protein to a host protein and decreases HIV infection in which the host protein is "encoded by a human Rab9 target sequence" as required by amended claim 46 (and all claims that depend therefrom).

As stated by the Office, "Wu *et al.* does not teach host protein Rab9." The additional references cited by the Office (Hanna *et al.*, Munzy *et al.* and Blot *et al.*) cannot and do not make up for the deficiencies in Wu *et al.* Nowhere do these references teach, suggest, or disclose that Rab9 binds to an HIV protein. The Office cites Blot *et al.* as allegedly teaching that "Rab9 bound to TIP47 interacts with the cytoplasmic tail of the HIV envelope protein subunit p41 and is critical for the incorporation of HIV envelope glycoprotein into mature virions." Office action page 4, line 21 – page 5, line 2. The Office cites the entire document as providing support for such statement. However, a detailed review of Blot *et al.* reveals that Rab9 is only mentioned on page 6934 of Blot *et al.* where it is disclosed that Rab9 binds to TIP47 and if residues $Ser^{167}ValVal$ were mutated to $Ala^{167}AlaAla$ the ability of TIP47 to bind Rab9 was decreased. Nowhere does this reference teach, suggest or disclose that Rab9 binds to the HIV1 envelope protein. The additional secondary references also do not teach this feature. Therefore, prior to

the present application it was not known that Rab9 could be used to identify compounds capable of decreasing HIV infection as presently claimed.

Because the cited references fail to teach or suggest (alone or in combination) all of the elements of the claims, they are not sufficient basis to support a rejection of the claims under 35 U.S.C. §103(a). Applicants respectfully request that these rejections be withdrawn.

One of Skill in the Art Could Not Have Predicted That Prior Art Could Have Been Modified with Reasonable Expectation of Success

An additional element of a *prima facie* case of obviousness is that the prior art must support a reasonable expectation of success for achieving the invention. "The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a *reasonable expectation* of success." M.P.E.P. § 2143.02 (emphasis added). The references cited in the rejection of the presently pending under 35 U.S.C. § 103(a) do not support a reasonable expectation of success for achieving the claimed invention. Therefore, the Office has not met this requirement for establishing *prima facie* obviousness, and the claims are allowable.

The Office asserts that one of ordinary skill in the art would have had a reasonable expectation of success in combining the cited references because "Wu provides evidence that laboratory methods involving cell signaling have been known in the art at the time of the present invention." Office action, page 5, lines 19-21. However, the Office has not shown how the identification of TIP47 as binding with HIV envelope 1 provides one of skill in the art with a *reasonable* expectation that Rab9 could be used in the assays of Wu *et al.* to identify modulators of HIV. As stated above, none of the references alone or in combination teach that Rab9 is capable of binding to an HIV protein. Thus, one of ordinary skill in the art could not have reasonably predicted that Rab9 could be used to identify compounds capable of decreasing HIV infection as presently claimed, if they didn't know Rab9 could bind an HIV protein.

Again, as stated in M.P.E.P. § 2143.02, "at least some degree of predictability is required" to support a finding of nonobviousness." Further, "whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time

the invention was made." M.P.E.P. § 2143.02. At the time of filing of the instant application, the ability of Rab9 to modulate HIV infectivity was not known. As such, at the time of filing, it was not possible to predict whether Rab9 could be substituted for CCR5 chemokine receptor to identify compounds that were capable of decreasing HIV infection because it was not even known to be an HIV modulator. Therefore, a finding that it would be obvious to substitute Rab9 for CCR5 chemokine in the assay provided by Wu *et al.* is not supported. Thus, the Office has not met its burden of showing a reasonable expectation of success for achieving the claimed invention to support the rejection of pending claims as obvious because one of skill in the art would *not* have had any reasonable expectation of success in achieving the Applicants' invention based on the cited references. Further, the combination of elements in the cited references did *not* yield predictable results in achieving the claimed invention.

As such, a *prima facie* case of obviousness has not been established and Applicants respectfully request the pending 35 U.S.C. §103(a) rejection to be withdrawn.

Conclusion

Applicants respectfully submit that the claims filed herewith are in condition for allowance. If any issues remain, Examiner Boesen is requested to contact the undersigned attorney to arrange a telephonic interview prior to the preparation of a subsequent action.

Respectfully submitted,

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